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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/147,490	05/13/1999	FREDERICK A. O. MENDELSOHN	016786/0215	1793

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FOLEY & LARDNER
3000 K STREET NW SUITE 500
PO BOX 25696
WASHINGTON, DC 200078696

EXAMINER
WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
1647	21

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/147,490	MENDELSOHN ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/10/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-24 and 26-33* is/are pending in the application.

4a) Of the above claim(s) *26,27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-24 and 28-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 May 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election with traverse of Species 1A ("modifying learning and facilitating memory retrieval") and Species 2A ("dementia") in Paper No. 20 (21 June 2003) is acknowledged. The traversal is on the ground(s) that the claims can be searched without undue burden. However, this has not been found persuasive because, as stated in the previous Office Action (Paper 19), the neuronal and biological activities differ in cell types, location and functional determinants, as well as animal models and methods of measurement. The diseases listed differ in etiologies and mechanisms, symptoms, treatments, patients, and treating personnel.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-3, 6-9 and 11-17 were withdrawn by the examiner in Paper 9 (30 February 2001). Claims 26 and 27 were withdrawn in Paper 13 (17 October 2001). Claims 1, 4, 5, 10 and 25 were cancelled by the applicant in Paper 12 (2 August 2001).

Claims 18-24 and 28-33, with Species 1A ("modifying learning and facilitating memory retrieval") and Species 2A ("dementia") are being examined in this Office Action.

Claim Rejections/Objections

Claim Objections

Claims 18 and 28 are objected to for reciting non-elected inventions.

Claim Rejections

35 *USC § 112, first paragraph - lack of enablement*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 18-24 and 28-33 are rejected under 35 U.S.C. 112, first paragraph, because the subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for the limitations of the claims wherein *LVV-Hemorphin* (SEQ ID NO: 1) is used for modulating a biological activity, such as "modifying learning and facilitating memory retrieval" or treating "dementia."

Claims 18-24 and 28-33 are drawn to a method of treating a patient or animal with a neuroactive peptide *LVV-Hemorphin-7* (SEQ ID NO: 1) in order to modulate neuronal activity. Dependent claims recite biological activities such as "modifying learning" and "[treating] dementia" and disease conditions. Additional claims recite vasoactive effects of the peptide, as well as substitutions of D-amino acids and other amino acid analogs into the *LVV-Hemorphin* peptide.

The specification discloses using *LVV-Hemorphin-7* to inhibit the amnesia caused by scopolamine in rats. Tests were conducted using passive-avoidance conditioning (page 28) and acquisition of a water maze (page 30), both typical methods of testing conditioning and learning in rats. A dose of the acetylcholine antagonist scopolamine immediately before each day's test

worsened the performance of the animals in learning shock-avoidance (passive-avoidance test) or in learning a spatial map (water maze). This amnesia lasted about 24 hours. The worsening of performance in rats was reversed by injection of *LVV-Hemorphin-7* prior to testing.

A sufficient amount of direction or guidance is lacking in claims 18-24 and 28-33. The specification gives examples wherein administration of *LVV-Hemorphin-7* reversed the temporary amnesia caused by scopolamine. That an acetylcholine antagonist causes a short-lasting amnesia is not surprising, given that acetylcholine has been shown linked to both long and short-term memory (Furey, et al, 1997, Proc. Natl. Acad. Sci., 94: 6512-6516) and given that cholinergic neurons are numerous in the hippocampus and in regions of the cortex involved in memory. Similarly, it is likely that a drug that physiologically inhibits the temporary amnesia caused by scopolamine would improve performance on tasks used to study short-term memory, acute memory, or consolidation to long-term memory, when such memory processes are inhibited by scopolamine (see, for example: Peng, et al, 1997, Jpn. J. Pharmacol., 74: 261-266). However, the quantity of experimentation required to use *LVV-Hemorphin-7* to treat a neuronal condition in humans or in animals is immense. For example, it is not known the neurological condition that scopolamine is intended to model. Few memory-related conditions recover spontaneously in 24 hours (see Figure 15, Specification). *Dementia*, for example, although encompassing several important diseases, is extremely complex as far as underlying causes, but is primarily a result of permanent changes in the central nervous system such as widespread neuron loss (Pearlman and Collins, Neurobiology of Disease, 1990, pages 306-308). Furthermore, whereas amnesia superficially resembles the memory loss seen in dementias, intellectual capacities remain intact (page 307, Pearlman and Collins, 1990). In the instant

Specification, two tests of short-term memory were conducted in which scopolamine appeared to have an amnesic effect in rats: the passive-avoidance test and the water maze. However nowhere in the specification is a nexus described between scopolamine administration and a model of modifying learning or dementia in mammals, including humans. It is difficult to imagine many human syndromes that would correlate with the rat model of temporary amnesia presented. The predictability of the art would be very low with regard to the results of inhibiting neuronal cell loss in a progressive and complicated syndrome such as dementia, for example. There are several enzymes and receptors involved in the neuronal loss, and the direct damage to cells is caused by chronic conditions such as arteriosclerosis or deposition of β-amyloid- to name two common examples- not by temporary inhibition of acetylcholine.

In summary, the specification does not provide a description of a repeatable process of modulating neuronal activity in a mammal or human by administering *LVV-Hemorphin-7* in such a way as to modulate a biological activity. Undue experimentation would be required to determine a disease for which scopolamine administration was an accurate model, as well as effective methods of modifying learning and facilitating memory retrieval or of treating dementia.

Due to the large quantity of experimentation required to: determine how to use a scopolamine inhibitor to ameliorate a neurodegenerative disorder or facilitate learning and memory; the lack of direction or guidance in the specification regarding the same; the lack of working examples in which *LVV-Hemorphin-7* was used to treat a complex disorder related to neuronal activity; the state of the art showing the complexities of neurodegenerative disorders; and the breadth of the claims which embrace many types of central nervous system disorders, --

undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, first paragraph – Written Description.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 30-33 are directed to the *LVV-Hemorphin-7* peptide of SEQ ID NO: 1 comprising one or more D-amino acids, non-naturally occurring amino acids, and/or amino acid analogues.

The specification as originally filed does not provide adequate written description for an isolated peptide of 10 amino acids wherein one or more of the amino acids are modified, while still maintaining the function of the *LVV-Hemorphin-7* polypeptide. This limitation is not expressly asserted nor does it flow naturally from the specification as originally presented.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The specification as originally filed does not provide adequate written description of the subgenus now claimed. The specification teaches the *LVV-Hemorphin-7* polypeptide of SEQ ID NO: 1. However, functional assays of modified *LVV-Hemorphin-7* polypeptide were not performed. The specification does not provide adequate support for a peptide of SEQ ID NO: 1 in which substitutions were made in one or more residues, said peptide retaining the function of *LVV-Hemorphin-7*.

Therefore, only a peptide of SEQ ID NO: 1 as disclosed in the Specification, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

Claims 18-24 and 28-33 are rejected for the reasons cited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The

examiner can normally be reached Monday - Friday from 9:30 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Sandra Wegert

8/12/03

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER